

CLAIMS

1. A combination product comprising at least one antisense oligonucleotide of the gene encoding MBD2 demethylase and at least one agent used in antitumor chemotherapy, for simultaneous, separate or prolonged use intended for the treatment of proliferative and inflammatory diseases.
- 10 2. The combination product as claimed in claim 1, characterized in that the antisense of the gene encoding MBD2 demethylase comprises at least:
 - 15 a) 15 consecutive nucleotides of the sequence SEQ ID No.1 or of the sequence complementary thereto, or of the sequence SEQ ID No.2, or
 - b) a sequence capable of hybridizing selectively with one of the sequences defined in a).
- 20 3. The combination product as claimed in either of claims 1 and 2, characterized in that the agent used in antitumor chemotherapy is selected from compounds belonging to the bleomycin family, in particular bleomycin.
- 25 4. The combination product as claimed in either of claims 1 and 2, characterized in that the agent used in antitumor chemotherapy is selected from antineoplastic agents capable of methylating DNA, in particular from methylating agents, such as streptozotocin, procarbazine, dacarbazine and temozolomide.

5. The combination product as claimed in either of claims 1 and 2, characterized in that the agent used in antitumor chemotherapy is selected from chloroethylating agents, in particular the chloroethylating agents:

1-(2-chloroethyl)-3-(2-hydroxyethyl)-1-nitrosourea,

10 1,3-bis(2-chloroethyl)-1-nitrosourea,

1-(2-chloroethyl)-3-(4-amino-2-methyl-5-pyrimidinyl)methyl-1-nitrosourea,

15 1-(2-chloroethyl)-3-cyclohexyl-1-nitrosourea,

1-(2-chloroethyl)-3-(4-methylcyclohexyl)-1-nitrosourea,

20 1-[N-(2-chloroethyl)-N-nitrosoureido]ethylphosphonic acid diethyl ester,

2-chloroethylmethylsulfonylmethanesulfonate.

6. The combination product as claimed in either of claims 1 and 2, characterized in that the agent used in antitumor chemotherapy is selected from:

25 - the various cytolytics such as dacarbazine, hydroxycarbamide, asparaginase, mitoguazone and plicamycin,

30 - the pro-apoptotic agents selected from glucocorticoid derivatives, topoisomerase inhibitors such as topoisomerase 2 inhibitors, for example anthracyclines, epipodophyllotoxin, such as etoposide, topoisomerase 1 inhibitors,

for example camptothecin derivatives,

- the antimetabolites such as antifolates, for example methotrexate, antipurines, for example 6-mercaptopurine, antipyrimidines, for example 5-fluorouracil,
- from the antimitotics such as the vinca-alkaloids, taxoids such as taxotere.

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7. The combination product as claimed in one of claims 1 to 6, characterized in that the antisense oligonucleotide of the gene encoding MBD2 demethylase is carried by a vector comprising a promoter which allows its effective expression in a eukaryotic cell.

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8. The combination product as claimed in one of claims 7, characterized in that it comprises a poly A transcription termination sequence.

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9. The combination product as claimed in claim 7, characterized in that the vector consists of a plasmid.

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10. The combination product as claimed in one of claims 1 to 8, characterized in that the antisense oligonucleotide is a double-stranded DNA.

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11. The combination product as claimed in one of claims 1 to 10, characterized in that it also comprises one or more elements which promote the transfer of the antisense oligonucleotide into the target cells.

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12. The combination product as claimed in one of claims 1 to 11, characterized in that the antisense oligonucleotide is suitable for administration in vivo

by electrotransfer, preferably using weak electric fields of between 1 and 600 V/cm.

13. The combination product as claimed in one of claims 1
5 to 12, characterized in that it also comprises one or more pharmaceutically acceptable vehicle(s).

14. The combination product as claimed in one of claims 1 to 13, in particular for simultaneous, separate or
10 prolonged use intended for the treatment of cancer.

15. The combination product as claimed in one of claims 1 to 14, characterized in that it is suitable for administration by intratumor injection.